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My46 Trait Profile

Argininosuccinic aciduria

Other Names: Argininosuccinate lyase deficiency

Argininosuccinic acidemia is a rare condition caused by the body's inability to fully break down argininosuccinic acid into arginine and fumarate. It is caused by mutations in the ASL gene that make the enzyme argininosuccinate lyase.

Characteristics of Argininosuccinic aciduria

Argininosuccinic aciduria is a genetic condition in which the body cannot metabolize (i.e., breakdown and use) argininosuccinic acid properly. As a result, other compounds, specifically ammonia, can build up in the body and brain. Too much ammonia can be harmful to the body and cause severe health problems including swelling of the brain and high liver enzymes or proteins.

There are two forms of argininosuccinic aciduria, a severe form occurring during infancy and a late onset form. In the severe, early onset form of this condition, infants may have vomiting, lethargy (low energy), poor feeding and hypothermia (a lower body temperature than normal). If not treated, seizures, intellectual disability, lethargy, coma and death may occur. Individuals with a later onset form, occurring in childhood, may have occasional high levels of ammonia during severe infections or other medical stresses. Over time, multiple events causing high levels of ammonia may result in impaired brain function, behavior abnormalities or learning disabilities.

Other characteristics that may occur include liver disease, and high blood pressure. Individuals with argininosuccinic aciduria may have coarse brittle hair called trichorrhexis nodosa that occurs when they are missing an important protein called arginine.

Diagnosis/Testing

Most individuals with argininosuccinic aciduria have changes or mutations in the ASL gene. This gene makes the argininosuccinate lyase enzyme that is responsible for breaking down argininosuccinic acid into arginine and fumarate. Mutations in the ASL gene that cause the enzyme to not be made or to not be made properly result in many of the health problems seen in individuals with argininosuccinic aciduria.

Many babies with argininosuccinic aciduria are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby's heel, and looks to see if the argininosuccinate lyase is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly genetic testing of the ASL gene.

Management/Surveillance

Individuals with argininosuccinic aciduria are typically managed by a team of specialty providers that may include: geneticists, genetic counselors, primary care doctors, dietitians/nutritionists, and social workers. Protein is found in many of the foods we eat, including breast milk and infant formulas. This means it is very important for individuals with argininosuccinic aciduria to follow a customized low-protein diet. This diet usually includes a medical formula specially made to provide only essential amino acids to limit the amount of nitrogen (building block for ammonia) in the diet and to ensure good nutrition. Specific supplements (i.e., arginine) and medications (referred to "ammonia scavengers") are also prescribed.

It is recommended that an emergency treatment plan, often documented by an "Emergency Letter" is made to ensure that during times of illness or other metabolic stress, a child with argininosuccinic aciduria will be assessed for signs and symptoms of a metabolic crisis (e.g., poor feeding, vomiting, lethargy, excessive sleepiness, irritability) and given appropriate medical attention. It is of upmost importance that individuals with argininosuccinic aciduria adhere to their specific diet and treatment plans to avoid metabolic stress and/or crisis.

Frequent monitoring is an essential part of the treatment and includes evaluating growth parameters; measuring ammonia, plasma amino acids and other indicators of levels of protein in the blood; and, evaluating nutritional status by measuring dietary intake.

Mode of inheritance

Argininosuccinic aciduria is inherited in an autosomal recessive pattern. This means that an individual has to inherit two ASL mutations (i.e., one from each parent) to be affected with argininosuccinic aciduria. If both parents are carriers of an ASL mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with argininosuccinic aciduria. Babies born in the United States are screened for argininosuccinic aciduria by newborn screening.

Risk to family members

Parents of a child with argininosuccinic aciduria are carriers of ASL mutations. If a sibling of a child with argininosuccinic aciduria is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of argininosuccinic aciduria.

Special considerations

None

Resources

Children Living with Inherited Metabolic Diseases
http://www.climb.org.uk
Genetics Home Reference: Argininosuccinic aciduria
http://ghr.nlm.nih.gov/condition/argininosuccinic-aciduria
National Urea Cycle Disorders Foundation
http://www.nucdf.org/
Newborn Screening Information
http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAL.html

References

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